

**AMENDMENTS TO THE SPECIFICATION**

Please replace the paragraph beginning at page 14, line 14, with the following amended paragraph.

Two receptors that bind to IL-17 like polypeptide of the present invention have been identified in Example 8 and are denoted as IL-17RB-2 and IL-17RB-3. Their nucleotide and amino acid sequences are set forth in SEQ ID NOS: 17-18 (IL-17RB-2) and SEQ ID NOs: 19-20 (IL-17RB-3), respectively. The predicted transmembrane domain spans residues 293 to 313 of SEQ ID NO: 18 and residues 351 to 371 of SEQ ID NO: 20. The predicted signal peptide spans 14 residues of SEQ ID NOS: 18 and 20. Therefore the predicted extracellular sequence spans amino acids 14 to 292 of SEQ ID NO: 18 and amino acids 14 to 350 of SEQ ID NO: 20. These receptors and are further described and characterized in co-owned, concurrently filed United States patent application serial no. 09/810,927 (Attorney Docket No. 01017/36917A) and in previously filed U.S. Patent Application serial nos. 09/723,232 filed November 27, 2000, U.S. provisional patent application serial no. 60/189,923 filed March 16, 2000 and U.S. provisional application serial no. 60/204,208 filed May 12, 2000, the disclosures of all of which are incorporated herein by reference in their entirety.

Please replace the paragraph beginning at page 21, line 15, with the following amended paragraph.

The terms ~~““AGP-XXXIL-17 “IL-17 like gene” or ““AGP-XXXIL-17 “IL-17 like nucleic acid molecule” or ““polynucleotide”~~ “polynucleotide” refers to a nucleic acid molecule comprising or consisting of a nucleotide sequence as set forth in SEQ ID NO: 1, SEQ ID NO:3, or SEQ ID NO:9, a nucleotide sequence encoding the polypeptide as set forth in SEQ ID NO: 2, SEQ ID NO:4, or SEQ ID NO:10, and nucleic acid molecules as defined herein.

Please replace the paragraph beginning at page 22, line 3, with the following amended paragraph.

The term ~~“AGP-XXX-IL-17”~~ “IL-17 like polypeptide allelic variant” “variant” refers to one of several possible naturally occurring alternate forms of a gene occupying a given locus on a chromosome of an organism or a population of organisms.

Please replace the paragraph beginning at page 22, line 15, with the following amended paragraph.

The term ~~“IL-17 like polypeptide fragment”~~ “IL-17 like polypeptide fragment” refers to a polypeptide that comprises a truncation at the amino terminus (with or without a leader sequence) and/or a truncation at the carboxy terminus of the polypeptide as set forth in SEQ ID NO: 2, SEQ ID NO:4, or SEQ ID NO:10, IL-17 like polypeptide allelic variants, IL-17 like polypeptide orthologs, IL-17 like polypeptide splice variants and/or an IL-17 like polypeptide variant having one or more amino acid additions or substitutions or internal deletions (wherein the resulting polypeptide is at least ~~six~~ six (6) amino acids or more in length) as compared to the IL-17 like polypeptide amino acid sequence set forth in SEQ ID NO: 2, SEQ ID NO:4, or SEQ ID NO:10. IL-17 like polypeptide fragments may result from alternative RNA splicing or from *in vivo* protease activity. In preferred embodiments, truncations comprise about 10 amino acids, or about 20 amino acids, or about 50 amino acids, or about 75 amino acids, or about 100 amino acids, or more than about 100 amino acids. The polypeptide fragments so produced will comprise about 25 contiguous amino acids, or about 50 amino acids, or about 75 amino acids, or about 100 amino acids, or about 150 amino acids, or about 200 amino acids. Such IL-17 like polypeptide fragments may optionally comprise an amino terminal methionine residue. It will be appreciated that such fragments can be used, for example, to generate antibodies to IL-17 like polypeptides.

Please replace the paragraph beginning at page 23, line 13, with the following amended paragraph.

The term ~~“AGP-XXX-like fusion polypeptide”~~ “IL-17 like fusion polypeptide” refers to a fusion of one or more amino acids (such as a heterologous peptide or polypeptide) at the amino or carboxy terminus of the polypeptide as set forth in SEQ ID NO:

NO:2, SEQ ID NO:4, or SEQ ID NO:10, IL-17 like polypeptide allelic variants, IL-17 like polypeptide orthologs, IL-17 like polypeptide splice variants, or IL-17 like polypeptide variants having one or more amino acid deletions, substitutions or internal additions as compared to the IL-17 like polypeptide amino acid sequence set forth in SEQ ID NO: 2, SEQ ID NO:4, or SEQ ID NO:10.

Please replace the paragraph beginning at page 23, line 26, with the following amended paragraph.

The term ~~““AGP-XXXIL-17-”~~ “IL-17 like polypeptide ortholog” ortholog” refers to a polypeptide from another species that corresponds to an IL-17 like polypeptide amino acid sequence as set forth in SEQ ID NO: 2, SEQ ID NO:4, or SEQ ID NO:10. For example, mouse and human IL-17 like polypeptides are considered orthologs of each other.

Please replace the paragraph beginning at page 24, line 1, with the following amended paragraph.

The term ~~““AGP-XXXIL-17-like polypeptide splice variant”~~ “IL-17 like polypeptide splice variant” refers to a nucleic acid molecule, usually RNA, which is generated by alternative processing of intron sequences in an RNA transcript of IL-17 like polypeptide amino acid sequence as set forth in SEQ ID NO: 2, SEQ ID NO:4, or SEQ ID NO:10.

Please replace the paragraph beginning at page 26, line 3, with the following amended paragraph.

The term “identity” as known in the art, refers to a relationship between the sequences of two or more polypeptide molecules or two or more nucleic acid molecules, as determined by comparing the sequences. In the art, “identity” also means the degree of sequence relatedness between nucleic acid molecules or polypeptides, as the case may be, as determined by the match between strings of two or more nucleotide or two or more amino acid sequences. “Identity” measures the percent of identical matches between the smaller of two or more sequences with gap alignments (if any) addressed by a particular mathematical model or computer program (*i.e.*, “algorithms”).~~“algorithms”~~.

Please replace the paragraph beginning at page 26, line 17, with the following amended paragraph.

The term “similarity” is a related concept, but in contrast to ~~“identity,” “similarity” is a related concept but, in contrast to~~ “identity”, refers to a measure of similarity which includes both identical matches and conservative substitution matches. If two polypeptide sequences have, for example, 10/20 identical amino acids, and the remainder are all non-conservative substitutions, then the percent identity and similarity would both be 50%. If, in the same example, there are ~~5~~five ~~five~~ more positions where there are conservative substitutions, then the percent identity remains 50%, but the per cent similarity would be 75% (15/20). Therefore, in cases where there are conservative substitutions, the degree of percent similarity between two polypeptides will be higher than the percent identity between those two polypeptides.

Please replace the paragraph beginning at page 28, line 3, with the following amended paragraph.

The term ~~“maturemature~~ “mature IL-17 like polypeptide” polypeptide” refers to an IL-17 like polypeptide lacking a leader sequence. A mature IL-17 like polypeptide may also include other modifications such as proteolytic processing of the amino terminus (with or without a leader sequence) and/or the carboxy terminus, cleavage of a smaller polypeptide from a larger precursor, N-linked and/or O-linked glycosylation, and the like. An exemplary mature human IL-17 like polypeptide can be found within the amino acid sequence of SEQ ID NO:2. An exemplary mature mouse IL-17 like polypeptide can be found within the amino acid sequence of SEQ ID NO:4 and SEQ ID NO:10. The term “nucleic acid sequence” or “nucleic acid molecule” ~~refer terms “nucleic acid sequence” or “nucleic acid molecule”~~ refer to a DNA or RNA sequence. ~~The term encompasses terms~~ terms encompass molecules formed from any of the known base analogs of DNA and RNA such as, but not limited to 4-4-acetylcytosine, 8-hydroxy-N6-methyladenosine, aziridinyl-cytosine, pseudoisocytosine, 5-(carboxyhydroxymethyl) uracil, 5-fluorouracil, 5-bromouracil, 5-carboxymethylaminomethyl-2-thiouracil, 5-carboxy-methylaminomethyluracil, dihydrouracil, inosine, N6-iso-pentenyladenine, 1-methyladenine, 1-methylpseudouracil, 1-methylguanine, 1-methylinosine, 2,2-dimethyl-guanine, 2-

methyladenine, 2-methylguanine, 3-methylcytosine, 5-methylcytosine, N6-methyladenine, 7-methylguanine, 5-methylaminomethyluracil, 5-methoxymino-methyl-2-thiouracil, beta-D-mannosylqueosine, 5' -methoxycarbonyl-methyluracil, 5-methoxyuracil, 2-methylthio-N6-isopentenyladenine, uracil-5-oxyacetic acid methylester, uracil-5-oxyacetic acid, oxybutoxosine, pseudouracil, queosine, 2-thiocytosine, 5-methyl-2-thiouracil, 2-thiouracil, 4-thiouracil, 5-methyluracil, N-uracil-5-oxyacetic acid methylester, uracil-5-oxyacetic acid, pseudouracil, queosine, 2-thiocytosine, and 2,6-diaminopurine.

Please replace the paragraph beginning at page 29, line 18, with the following amended paragraph.

The term ~~[[“]]~~“operably linked” ~~operably-linked~~” is used herein to refer to an ~~arrangement~~arrangement method of flanking sequences wherein the flanking sequences so described are configured or assembled so as to perform their usual function. Thus, a flanking sequence operably linked to a coding sequence may be capable of effecting the replication, transcription and/or translation of the coding sequence. For example, a coding sequence is operably linked to a promoter when the promoter is capable of directing transcription of that coding sequence. A flanking sequence need not be contiguous with the coding sequence, so long as it functions correctly. Thus, for example, intervening untranslated yet transcribed sequences can be present between a promoter sequence and the coding sequence, and the promoter sequence can still be considered ~~[[“]]~~“operably linked” ~~operably-linked~~” to the coding sequence.

Please replace the paragraph beginning at page 30, line 25, with the following amended paragraph.

The term “transduction” ~~“transduction”~~ is used to refer to the transfer of genes from one bacterium to another, usually by a phage. “Transduction” ~~“Transduction”~~ also refers to the acquisition and transfer of eukaryotic cellular sequences by retroviruses.

Please replace the paragraph beginning at page 30, line 31, with the following amended paragraph.

The term ~~[[“]]~~“transfection” ~~”transfection”~~ is used to refer to the uptake of foreign or exogenous DNA by a cell, and a cell has been “transfected” ~~“transfected”~~ when the exogenous DNA has been introduced inside the cell membrane. A number of transfection techniques are well known in the art and are disclosed herein. See, for example, Graham et al., Virology, 52:456 (1973); Sambrook et al., Molecular Cloning, a ~~laboratory~~ Laboratory Manual, Cold Spring Harbor Laboratories (New York, 1989); Laboratories, New York, (1989); Davis et al., Basic Methods in Molecular Biology, Elsevier, 1986;(1986); and Chu et al., Gene, 13:197 (1981). Such techniques can be used to introduce one or more exogenous DNA moieties into suitable host cells.

Please replace the paragraph beginning at page 31, line 14, with the following amended paragraph.

The term “transformation” ~~“transformation”~~ as used herein refers to a change in a cell’s genetic characteristics, and a cell has been transformed when it has been modified to ~~contains~~ contained a new DNA. For example, a cell is transformed where it is genetically modified from its native state. Following transfection or transduction, the transforming DNA may recombine with that of the cell by physically integrating into a chromosome of the cell, it may be maintained transiently as an episomal element without being replicated, or ~~[[I]]~~ may replicate independently as a plasmid. A cell is considered to have been stably transformed when the DNA is replicated with the division of the cell.

Please replace the paragraph beginning at page 31, line 28, with the following amended paragraph.

The term “vector” ~~“veeter”~~ is used to refer to any molecule (e.g., nucleic acid, plasmid, or virus) used to transfer coding information to a host cell.

Please replace the paragraph beginning at page 36, line 29, with the following amended paragraph.

Conservative modifications to the amino acid sequence of SEQ ID NO: 2, ~~(and the NO:2, SEQ ID NO:4, or SEQ ID NO:10~~ (and corresponding modifications to the encoding nucleotides) will produce IL-17 like polypeptides having functional and chemical characteristics similar to those of a naturally occurring IL-17 like polypeptide. In contrast, substantial modifications in the functional and/or chemical characteristics of IL-17 like polypeptides may be accomplished by selecting substitutions in the amino acid sequence of SEQ ID NO: 2, SEQ ID NO:4, or SEQ ID NO:10 that differ significantly in their effect on maintaining (a) the structure of the molecular backbone in the area of the substitution, for example, as a sheet or helical conformation, (b) the charge or hydrophobicity of the molecule at the target site, or (c) the bulk of the side chain.

Please replace the paragraph beginning at page 37, line 14, with the following amended paragraph.

For example, a ~~“conservative amino acid substitution”~~ “conservative amino acid substitution” may involve a substitution of a native amino acid residue with a nonnative residue such that there is little or no effect on the polarity or charge of the amino acid residue at that position. Furthermore, any native residue in the polypeptide may also be substituted with alanine, as has been previously described for ~~“alanine”~~ “alanine scanning mutagenesis.” ~~mutagenesis.”~~

Please replace the paragraph beginning at page 37, line 23, with the following amended paragraph.

Desired amino acid substitutions (whether conservative or non-conservative) can be determined by those skilled in the art at the time such substitutions are desired. For example, amino acid substitutions can be used to identify important residues of the AGP-~~XXX~~ IL-17 like polypeptide, or to increase or decrease the affinity of the AGP-~~XXX~~ IL-17 like polypeptides described herein.

Please replace the paragraph beginning at page 39, line 18, with the following amended paragraph.

For example, non-conservative substitutions may involve the exchange of a member of one of these classes for a member from another class. Such substituted residues may be introduced into regions of the human ~~AGP~~-IL-17 like polypeptide that are homologous with non-human IL-17 like polypeptide orthologs, or into the non-homologous regions of the molecule.

Please replace the paragraph beginning at page 79, line 11, with the following amended paragraph.

Additionally, the ~~AGP-XXX like~~ IL-17-like polypeptide may be purified ~~through the~~ through the use of a monoclonal antibody which is capable of specifically recognizing and binding to the ~~AGP-XXX like~~ IL-17-like polypeptide.

Please replace the paragraph beginning at page 85, line 19, with the following amended paragraph.

Generally, conditions which may be alleviated or modulated by the administration of the present IL-17 like polypeptide derivatives include those described herein for IL-17 like polypeptides. However, the ~~AGP-~~ IL-17 like polypeptide derivatives disclosed herein may have additional activities, enhanced or reduced biological activity, or other characteristics, such as increased or decreased half-life, as compared to the non-derivatized molecules.

Please replace the paragraph beginning at page 88, line 7, with the following amended paragraph.

This high throughput expression profiling has a broad range of applications with respect to the ~~AGP-XXX like~~ IL-17-like molecules of the invention, including, but not limited to: the identification and validation of IL-17-like ~~XXX~~ disease-related genes as targets for therapeutics; molecular toxicology of ~~AGP-XXX like~~ IL-17-like molecules and inhibitors thereof; stratification of populations and generation of surrogate markers for clinical trials; and ~~enhancing AGP-XXX like related~~ the enhancement of an IL-17-like related



small molecule drug discovery by aiding in the identification of selective compounds in high throughput screens (HTS).

Please replace the paragraph beginning at page 93, line 25, with the following amended paragraph.

Competitive binding assays rely on the ability of a labeled standard (*e.g.*, an IL-17 like polypeptide, or an immunologically reactive portion thereof) to compete with the test sample analyte (an IL-17 like polypeptide) for binding with a limited amount of ~~anti~~ ~~AGP-XXX~~ anti- IL-17 like antibody. The amount of an IL-17 like polypeptide in the test sample is inversely proportional to the amount of standard that becomes bound to the antibodies. To facilitate determining the amount of standard that becomes bound, the antibodies typically are insolubilized before or after the competition, so that the standard and analyte that are bound to the antibodies may conveniently be separated from the standard and analyte which remain unbound.

Please replace the paragraph beginning at page 97, line 6, with the following amended paragraph.

In some situations, it may be desirable to identify molecules that are modulators, *i.e.*, agonists or antagonists, of the activity of IL-17 like polypeptide. Natural or synthetic molecules that modulate IL-17 ~~XXX~~ like polypeptide may be identified using one or more screening assays, such as those described herein. Such molecules may be administered either in an *ex vivo* manner, or in an *in vivo* manner by injection, or by oral delivery, implantation device, or the like.

Please replace the paragraph beginning at page 159, line 6 with the following amended paragraph.

The human IL-17 like cDNA (clone Origene-89) is 3987 bp in length and is set out as SEQ ID NO: 1. This cDNA was deposited as accession no. PTA-3470 with the American Type Culture Collection (10801 University Blvd. Manassas, VA 20110) on June 20, 2001 under the Budapest Treaty. This cDNA encodes an open reading frame of 161 amino acids with a predicted signal peptide of 16 amino acids and a predicted mature protein

of 145 amino acids (SEQ ID NO: 2). A FASTA search of the SwissProt database with the predicted IL-17 like protein sequence indicated that SEQ ID NO: 2 exhibited 25.0% identity within 160 amino acid overlap with IL-17, 36.7% identity within 90 amino acid overlap with IL-20, 35.6% identity within 90 amino acid overlap with IL-17B and 34.5% identity within 171 amino acid overlap with IL-17C. Similar to other IL-17 family members, the novel human IL-17 like polypeptide (also denoted IL-17E herein) is predicted to be a secreted protein and is predicted to be a cytokine.

Please replace the paragraph beginning at page 177, line 12 with the following amended paragraph.

The pCEP4-huIL-17RB-2 like-Fc plasmid or pCEP4-huIL-17RB-3 like-Fc plasmid (also denoted HIL-17RB-2-Fc and HIL17RB-3-Fc, respectively, and deposited on March 14, 2001 with the American Type Culture Collection, 10801 University Blvd., Manassas, VA 20110, U.S.A. under Accession Nos. PTA-3174 and PTA-3178, respectively) were transiently transfected into human 293/EBNA cells using Superfect (Qiagen) according to the manufacturer's instructions. The serum-free conditioned media was harvested from the cells 72 hours after transfection. The recombinant human IL-17RB like-Fc fusion proteins, predicted to have the amino acid sequence APS located at the amino-terminus of the mature protein, were isolated by affinity chromatography using a HiTrap Protein G column (Amersham Pharmacia). The amino acid sequences of the resulting fusion proteins are set out in as SEQ ID NOS: 21 and 22.

Please replace the paragraph beginning at page 178, line 21, with the following amended paragraph.

To determine if IL-17 like polypeptide is a ligand for the IL-17 receptor B (IL-17RB) polypeptides (SEQ ID NOS: 18 and 20), competitive binding assays were performed with the human B-lymphoblast cell line GM3104A which has been shown to express IL-17RB by Northern blot and RT-PCR analyses. The conditioned media from 293E cells transfected to express IL-17 like-Fc fusion protein (described above in Example 6) was collected, concentrated and used for the binding assay. Specificity of ligand binding was determined by competition with soluble blocking receptors, either IL-17RB-2 or IL-17RB-3. IL-17R-Fc fusion protein (containing the extracellular portion of IL-17 receptor) was purified

from conditioned media collected from transfected 293E cells. Conditioned media from 293E cells transfected with IL-17RB-2-Fc or IL-17-RB-3-Fc (deposited with the ATCC on March 14, 2001 under Accession Nos. PTA-3174 and PTA-3178 respectively) as described above in Example 7 was concentrated (5x) with an Amicon 3Kd cut-off Centracon (#4203) and also used for blocking.